

Elevated Serum Uric Acid Concentration In College Athletes: A Preliminary Study

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istration.

The factors controlling the metabolism of purines and their relationship to gout have been of continuing interest for investigators since Sheele isolated uric acid from urine in 1776.²¹ The incidence of gout in men of genius throughout history is well known and, apparently, women of genius have not been studied systematically. Recent studies^{1,15} have lent substantial support to the hypothesis that serum sodium urate concentration is related to achievement-oriented behavior, a factor of apparent major importance to those engaged in competitive sports. Older studies have shown that acute physical exercise of various intensity and duration induced a rise in serum uric acid in both men¹⁷ and women.²⁰ Recently, Dunn *et al.*⁶ observed a positive relationship in male high school students between serum urates and the degree of participation in combined scholastic and athletic activities, but essentially no relationship between urates and athletic participation alone. Recent results from the Framingham study over a period of 16 years on 2,283 men and 2,844 women between the ages of 30 and 59 indicated that gouty arthritis occurred in 1.8 per cent of those with serum uric acid concentrations between 6 and 6.9 mg/100 ml, in 11.8 per cent of those with levels between 7 and 7.9 mg/100 ml, and in 36 per cent of those with a urate concentration of 8 mg/100 ml and above.¹²

During the course of extensive medical examinations on a group of healthy Caucasian male college athletes who were to be test subjects in experiments involving heat, exercise and dehydration, high fasting serum uric acid concentrations were noted. Follow-up determinations confirmed the initial results. For comparative purposes, similar uric acid data were available from a group of female physical education teachers.

The purpose of this study was to investigate the serum uric acid concentrations of men and women who had participated regularly in physical activity for a number of years. The unexpected finding of elevated serum urates in 50 per cent or more of the men examined broaches some important questions. First, what is the relative influence of physical activity and/or genetic factors on the level of serum uric acid? Second, what kinds of people should constitute the population from which normal uric acid values are established? Third, what should be considered an elevated serum uric acid concentration? And lastly, what is the influence and contribution of individual variability to the serum uric acid concentration?

Methods

Twenty-nine healthy male college athletes, aged 21 to 31 (mean, 23) were studied by complete medical history, physical examination and laboratory tests. The latter tests, conducted with the subjects in a post-absorptive condition, included hemoglobin, hematocrit, white blood cell count and differential, VDRL serology, erythrocyte sedimentation rate, urinalysis, fasting blood sugar, serum uric acid, roentgenogram of the chest and an electrocardiogram. Special attention was directed to the presence of rheumatic disease, gout, renal lithiasis, drug intake, psoriasis, nutrition, alcoholic ingestion or hematologic dyscrasias in the subject or his family. Seven months later serum urate determinations were repeated on 20 (mean age, 24) of the original 29 men. Similar examinations were performed on 13 female physical education teachers, aged 24 to 33 (mean, 26) who had also participated in dehydration experiments.⁹ Since their uric acids were within the normal range for women, no follow-up determinations were done. The history and physical examinations of the men and women were performed by the same physician.

All uric acid determinations were performed at the Palo Alto Medical Clinic laboratory by the colorimetric method of Henry *et al.*¹³ The normal ranges of uric acid values in this laboratory were 3.5 to 6.0 mg/100 ml for males and 2.5 to 5.0 mg/100 ml for females. Control blood was analyzed daily and the maximum measurement error was ± 0.3 mg/100 ml. It should be noted that the colorimetric methods of measuring uric acid give higher values than enzymatic methods below 6.0 mg/100 ml and lower values above 6.0 mg/100 ml; this problem is discussed more fully elsewhere.²

Results

At the time of the first testing (TABLE I) 11 of 20 men (55 per cent) exhibited elevated serum urates (over 6.0 mg/100 ml). Seven months later 10 men showed this same result. The latter elevated values occurred despite the fact that the average urate concentration was 0.2 mg/100 ml lower than the first test. Of the original 29 cases, the highest and lowest urates were not included in the 20. The mean uric acid concentrations of the two groups remained approximately equal: 29 men = 6.1 ± 1.0 ; 20 men = 6.2 ± 0.9 mg/100 ml. Thus, the 20 were reasonably representative of the original 29 cases. When retested, six of the 11 cases that were *elevated* remained so and five reverted to the normal range. Six determinations that were *normal* remained so and three others became newly elevated.

TABLE I

Serum Uric Acid Concentrations in 20 Healthy Male College Athletes in the Present Study

Subject	Test 1 (Oct. 1965) mg/100 ml	Test 2 (May 1966) mg/100 ml	Difference
GA	6.4	6.2	-0.2
WBr	7.1	6.4	-0.7
WBU	6.9	5.8	-1.1
RB	4.7	4.5	-0.2
DC	6.9	5.8	-1.1
GD	6.5	6.7	+0.2
JF	7.7	6.0	-1.7
DF	5.7	5.0	-0.7
TG	5.9	5.1	-0.8
MH	6.3	6.9	+0.6
JM	5.4	6.2	+0.8
JMc	7.5	6.9	-0.6
PM	4.7	5.7	+1.0
RS	4.7	5.4	+0.7
FS1	5.7	6.5	+0.8
RSt	5.9	5.0	-0.9
WS	6.7	6.9	+0.2
LT	5.6	7.1	+1.5
RW	6.9	5.8	-1.1
JW	6.2	5.8	-0.4
Mean	6.2	6.0	
\pm S.D.	0.9	0.7	
Range	(4.7 to 7.7)	(4.5 to 7.1)	(-1.7 to +1.5)
% cases			
>5.9 mg/100 ml	55.0	50.0	
% cases			
>6.9 mg/100 ml	15.0	5.0	

A survey of the diets of these students indicated no large intake of purine-rich food or, with one exception, excessive alcohol consumption. The physical examinations were within normal limits and displayed no specific evidence of arthritis, gout or gouty tophi, splenomegaly, lymphadenopathy, purpura, petechiae, ecchymoses, or psoriasis. All other laboratory parameters were normal.

A comparison of data from the present report with other selected studies (TABLE II) indicated that not only did the present group of men have the highest mean urate concentration, but it also had the largest percentage of cases (51.7 per cent) with 6.0 mg/100 ml or over. Dunn *et al.*'s⁶ older executives had 43.3 per cent and Emmerson and Sandilands⁷ students had 32.0 per cent over 6.0 mg. The study of executives⁶ demonstrated that 16.5 per cent of their cases had 7.0 mg/100 ml or greater compared with 13.8 per cent in the present study; all other groups had lower values. These findings suggest that some factor other than emotional stress probably was contributing to the elevated urates in these athletes. Similar data from females in the present study were not remarkably different from that in the other comparative works (TABLE II).

TABLE II
Comparisons of Some Representative Serum Uric
Acid Values with Those of the Present Study

Reference	No. Cases	Occupation	Serum Uric Acid Conc. (mg/100 ml)			
		Age	(Mean±S.D.)	(Range)	(%>5.9)	(%>6.9)
MALES						
Mikkelsen et al. ¹⁸ (Americans)	2,987	Various 4-80+	4.9±1.4*	1.0 - 13.6	20.8	7.4
Mikkelsen et al. ¹⁸ (Americans)	153	Various 20-24	5.6±1.3*	2.6 - 13.6	28.8	11.1
Emmerson et al. ⁷ (Australians)	100	Students 20-30	5.6±1.0†‡	3.5 - 8.4	32.0	7.0
Dreyfuss et al. ⁵ (Israelis)	21	Students 20-30	5.4±1.1§	4.1 - 7.4	33.3	9.5
Dunn et al. ⁶ (Americans)	18♂+3♀ 331	Executives 40-60	5.7±1.2*	————	43.3	16.5
Dunn et al. ⁶ (Americans)	76	Ph.D. Scientists	5.3±1.2*	————	26.3	9.2
Dunn et al. ⁶ (Americans)	532	Craftsmen 40-60	4.8±1.1*	————	12.6	3.5
Present Study (Americans)	29	Students 21-31	6.1±1.0‡	3.6 - 11.4	51.7	13.8
FEMALES						
Mikkelsen et al. ¹⁸ (Americans)	3,013	Various 4-80+	4.2±1.2*	1.0 - 11.9	21.9	7.2
Mikkelsen et al. ¹⁸ (Americans)	277	Various 25-29	4.0±1.2*	1.0 - 11.6	16.2	5.4
Emmerson et al. ⁷ (Australians)	100	Nurses 20-25	4.5±0.7†‡	2.5 - 6.4	30.0	1.0
Present Study (Americans)	11	Teachers 24-33	4.6±0.7‡	3.0 - 6.4	27.3	9.1

*Liddle, L. et al., *J. Lab. Clin. Med.*, 54: 903, 1959.
(Enzymatic method)

†Feichtmeir, T. V., et al., *Am. J. Clin. Path.*, 25: 833, 1955.
(Enzymatic method)

‡Henry, R. J., et al., *Am. J. Clin. Path.*, 28: 152, 1957.
(Colorimetric method)

§Hepler, O. E., et al., *Am. J. Clin. Path.*, 22: 72, 1952.
(Colorimetric method)

Discussion

Possible explanations for the frequency of serum urate elevations in this group of male athletes might suggest: (1) that the upper limits of the normal range for serum uric acid are unrealistically low, and/or (2) there was something unique about the population under study.

The normal upper limits for serum uric acid are usually taken to be 6.0 mg/100 ml for men and 5.0 mg/100 ml for women. Recently, it has been suggested that the upper limits be increased to 7.0 mg/100 ml for males and about 6.0 mg/100 ml for females.^{3,7} The comparison of the percentage of cases over 5.9 and 6.9 mg/100 ml in TABLE II indicated a substantial elevation of serum urate in our group of men. Thus, the set-point of the upper limit of normal would not appreciably affect our conclusions. However, the set-point of the upper limit should reflect the optimal level for health, with due regard for individual variability, and it should not be increased solely on the basis of statistical calculations of a population whose urate concentration is rising progressively due, possibly, to undesirable influences.

There are many factors that seem to affect serum uric acid concentration in healthy people: age and

sex,¹⁸ drugs,⁸ diet,¹⁶ occupation and social class status,⁶ achievement oriented behavior and drive,⁴ physical exercise,^{17,20} and genetic factors.^{18,21} On the basis of case history and comparative data analyses the first four factors may be rejected and, consequently, our attention is directed to achievement oriented behavior, genetic factors and physical exercise.

Since these men were athletes in various stages of training and in active competition, the question arises whether the elevated urates could have been influenced by their repetitive, chronic exercise. It has been known for many years that acute, strenuous physical exercise is followed by a rather marked rise (2 to 3 mg/100 ml) in serum uric acid concentration.¹⁷ On the other hand light exercise increases serum urates only slightly (0.16 ± 0.07 mg/100 ml).²³ Hale *et al.*¹¹ observed significant elevations in uric acid excretion in men performing 12-hour sedentary flight simulation experiments. Moderate to strenuous exercise induces many of the physiologic and metabolic changes that favor elevated urates mainly by depression of urate excretion by the kidney: lacticacidemia is associated with a decreased uric acid excretion;¹⁹ B-hydroxybutyrate and sodium acetoacetate impair urate clearance;¹ a decreased urinary flow²² accentuated

by an inhibition of voluntary water intake due to exercise¹⁰ would retard uric acid excretion; and an increased turnover of tissue protein and erythrocytes¹⁴ could add additional nucleic acids to the purine pool.

It is possible that hyperuricemia may be, at least in part, a non-specific reaction to stress conditioned by genetic factors. That is, those individuals who are able to undertake college work may have a genetic predisposition for intelligence, drive, achievement and leadership as well as for elevated uric acid.^{4,15} Such individuals may also be drawn to athletics. However, the magnitude of the serum urates in our subjects was not directly associated with any acute, stressful situation. It is likely that all three factors operate to determine the final uric acid concentration. In the total population the highest serum urate concentration occurs in males in the 16-24 year age group, when men also engage in the heaviest physical exercise and athletic competitions.¹⁸ In a subsequent study we have observed a significant decrease in serum uric acid concentration in a group of athletes after a two-month training program.² In view of these findings, further investigation into the relationships between long-term athletic training, hyperuricemia and gout would seem imperative.

It is important to emphasize that in asymptomatic individuals elevated serum urates may exist that are not necessarily the reflection of a disease state. One way to evaluate these elevated serum urates is to obtain a baseline uric acid for comparison in later years. The study of serum uric acid concentrations in various "normal" populations must be ongoing and perhaps a re-definition of the normal range will be necessary eventually.

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